THE STRUCTURE
OF
HYALINE CARTILAGE.

WITH DEDUCTIONS REGARDING
THE CELL-DOCTRINE AND THE BIOPLASSON-DOCTRINE,
BEING THE FIRST CHAPTER OF "CONTRIBUTIONS TO THE HISTOLOGY OF THE CARTILAGES OF THE LARYNX."

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PROF. OF LARYNGOLOGY AND DISEASES OF THE THROAT IN DARTMOUTH MEDICAL COLLEGE.

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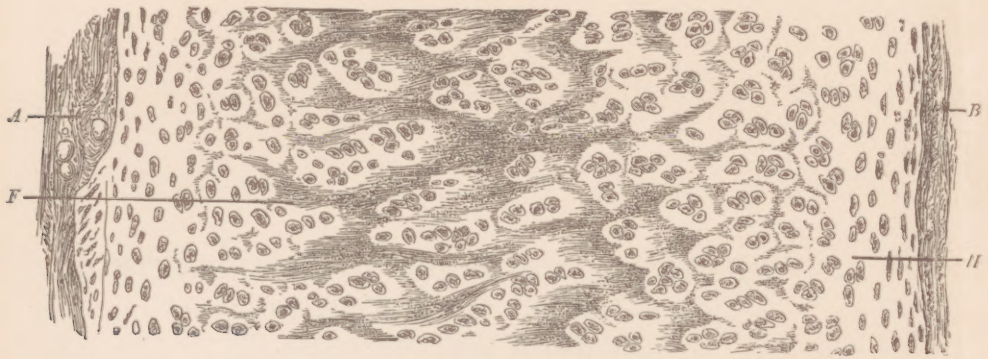

FIG. 1.

Plate of the Thyroid Cartilage of Adult. Longitudinal Section. x 100.
A.—Perichondrium toward the mucous membrane.
B.—Perichondrium toward the skin.
F.—Fibrous portion of cartilage in the centre.
H.—Hyaline portion, on either side, near the perichondrium.

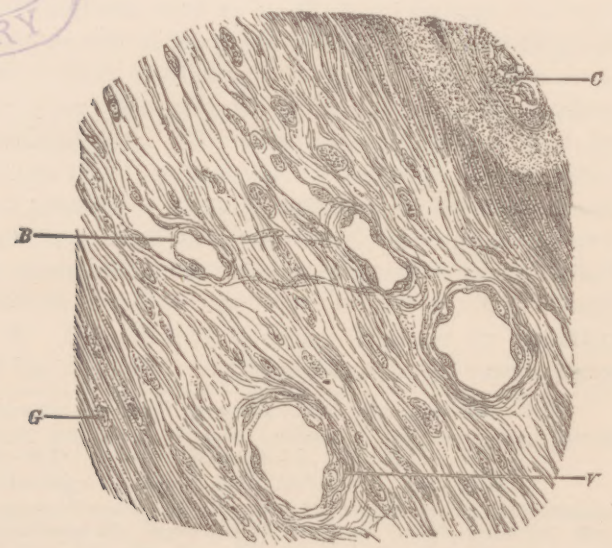

FIG. 2.

Fibrous Portion of Thyroid Cartilage. x 600.
C.—Cartilage corpuscle, surrounded by a dense basis-substance.
G.—Granules of living matter.
B.—Capillary blood-vessel.
V.—Small vein.

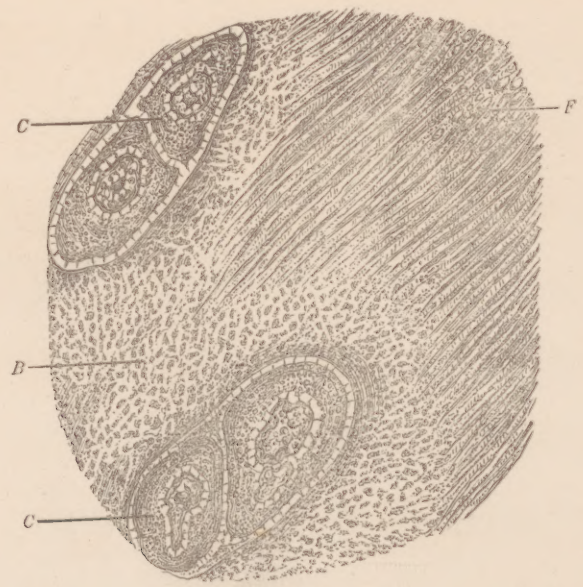

FIG. 3.

Thyroid Cartilage of Adult. Sagittal Section. x 1200.
C.—Cartilage corpuscles.
B.—Indistinctly reticular hyaline basis-substance.
F.—Fibrous basis-substance.

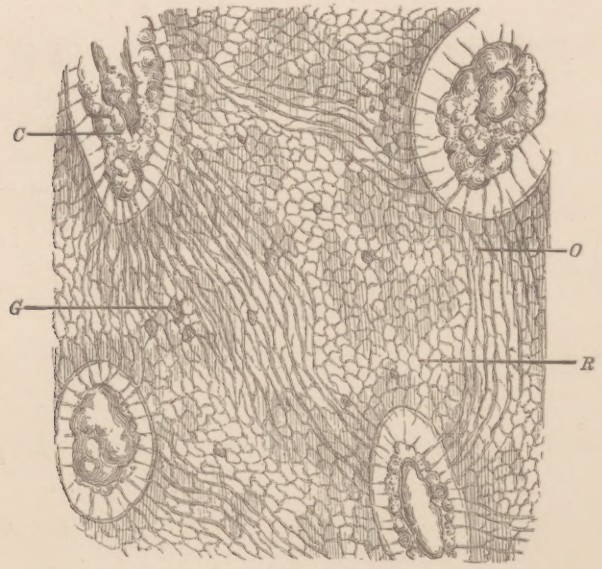

FIG. 4.

Thyroid Cartilage of Adult, kept in strong Alcohol. Horizontal Section. x 1200
C.—Shrivelled cartilage corpuscle.
O.—Longitudinal offshoots.
R.—Reticulum in basis-substance.
G.—Granules of living matter.

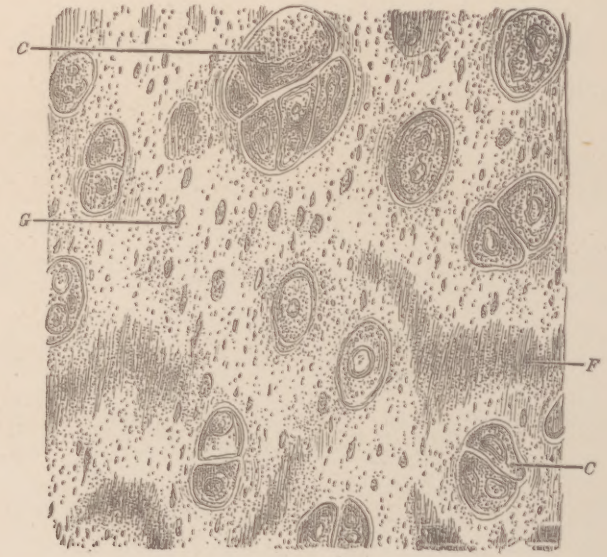

FIG. 5.

Thyroid Cartilage of Adult. Horizontal Section. x 600.
C.—Cartilage corpuscles.
F.—Fibrous portion of cartilage.
G.—Granules of living matter.

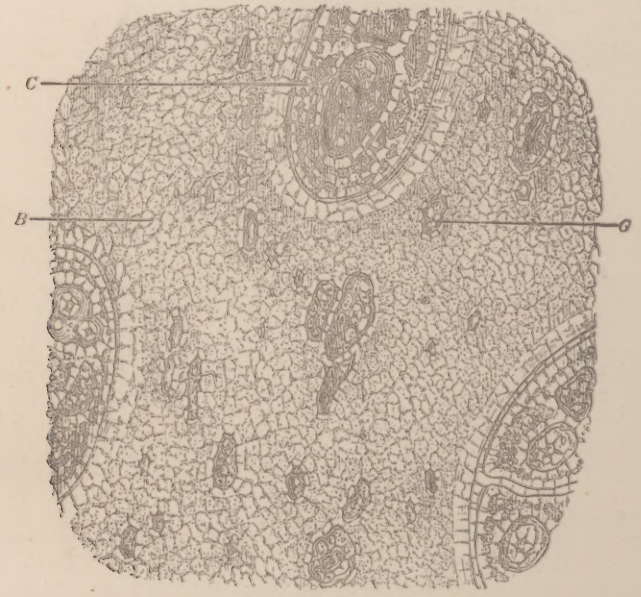

FIG. 6.

Thyroid Cartilage of Adult. Horizontal Section. x 1200.
C.—Cartilage corpuscle.
B.—Hyaline basis-substance.
G.—Granules of living matter.

CONTRIBUTIONS TO THE NORMAL AND PATHOLOGICAL HISTOLOGY OF THE CARTILAGES OF THE LARYNX.

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CHAPTER I.—ESSENTIAL STRUCTURE OF HYALINE CARTILAGE.*

SECTION I.—*Historical.*

FROM the earliest time of histology to the present, true cartilage, such as the thyroid cartilage, has been looked upon as one of the simplest tissues. To distinguish it from other kinds of cartilage, in which either a fibrous or a reticular aspect has been recognized, it is called hyaline, *i. e.*, resembling glass. The description of its structure, by MECKAUER in 1836,[1] is essentially as that by KLEIN in 1880,[2] viz., that it consists of a firm homogeneous basis-substance, in which are imbedded numerous small cartilage-corpuscles. Meckauer wrote before the cell-doctrine, which has exercised so powerful an influence upon the medical mind, had been thought of. Indeed, that doctrine itself, as its founder, Schwann,[3] has recorded, was based to a large extent upon

* Read before the American Laryngological Association, session 1881.

[1] De penitiori cartilaginum structura symbolæ. Diss. anat.-phys., auctore M. Meckauer, M.D. Breslau : Schultz & Co., 1836, Tab. 4, pp. 16.

[2] Atlas of Histology. London : Smith, Elder & Co., 1880, p. 48.

[3] Mikroskopische Untersuchungen über die Uebereinstimmung in der Structur und dem Wachsthume der Thiere und Pflanzen., von Dr. Th. Schwann. Berlin : G. E. Reimer, 1839, pp. 270. Microscopical researches into the accordance in the structure and growth of animals and plants. Translated by Henry Smith. London : Sydenham Society, 1847. Introduction.

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investigations of the constitution of cartilage. After J. Müller had described cartilage-corpuscles that were hollow, and Gurlt had spoken of some as vesicles, when Schwann had succeeded, as he thought, "in actually observing the proper wall of the cartilage-corpuscles, first in the branchial cartilages of the frog's larvæ, and subsequently also in the fish," he was led by these and other researches to conjecture "that the cellular formation might be a widely extended, perhaps a universal principle for the formation of organic substances."

Schwann considered that the cartilage-corpuscles, or cartilage-cells as they were thenceforth called, are imbedded in a matrix which is capable of producing the cells, and which he therefore called cytoblastema. Goodsir, Naegeli, and finally Virchow advanced the histology of cartilage in so far as they claimed that the cartilage-cells can not possibly arise from the matrix or intercellular substance. Even Virchow adhered, however, to the idea of Schwann, that the cartilage-cell is a vesicle filled with a more or less transparent fluid, in which is suspended the nucleus; and, although he was aware of the life of the cell in general, nothing was suggested by him as to the life of cartilage. It is true Donders and H. Meyer had observed that the cells of hyaline cartilage were capable of proliferation[1]; nevertheless the idea became prevalent, more perhaps from implication, because on account of the absence of blood-vessels it was believed not liable to inflammation, than from any direct statement to that effect, that cartilage was devoid of life. The vitality of cartilage-corpuscles was made clearly probable by the observation of the effect of electrical shocks upon them, by Heidenhain,[2] and by Rollett,[3] and the investigations of Reitz,[4] Boehm,[5] Hutob,[6] and Bub-

[1] (Mueller's) *Archiv für Anatomie*, 1846.

[2] Studien aus dem physiologischen Institut zu Breslau, ii Heft, 1863.

[3] Stricker's Handbuch der Lehre von den Geweben: Article "Knorpelgewebe," 1868.

[4] Sitzungsber. der K. K. Akademie der Wissensch. in Wien., Bd. 55, 1867.

[5] Beiträge zur normalen und pathologischen Anatomie der Gelenke. Inaug.-Dissertation, Würzburg, 1868.

[6] "Untersuchungen über Knorpelentzündung." *Wiener. med. Jahrbücher*, 1871, p. 399.

noff,[1]—investigations which, except Boehm's, were made under Stricker; it was proved positively by Heitzmann in 1873.[2]

With the question whether or not the so-called cartilage-"cell" is alive, another question arose, viz., how can so isolated a corpuscle (imbedded in a firm "intercellular" substance) obtain nutrition? It was assumed that the nourishing liquid reaches the corpuscle either by diffusion or else through canals, or clefts, or fissures in the homogeneous basis-substance. The idea of the existence of juice-channels originated with Von Recklinghausen. He found in silver-stained preparations of the cornea, communicating colorless spaces on a dark background, and believing that the cornea consisted of fibrillary tissue knit together by a cement-substance, he thought that this cement-substance was tunneled by a system of communicating-canals, "*Saft-Kanälchen*," and that it is this system of canals which is not stained by silver. Innumerable investigations, under all sorts of circumstances, have been undertaken to settle satisfactorily whether preformed juice-channels exist in cartilage, or whether juices can be imbibed without such. In lower animals corresponding canals had long been reported to be found, by Queckett[3] and by Bergmann[4] in cephalopodes, and by Leydig[5] in various fishes; and certain pathological observations by Virchow,[6] Zahn,[7] Cornil and Ranvier,[8] and Rindfleisch,[9] as well as senile changes studied by Weichselbaum,[10]

[1] Beiträge zur Kenntniss der Structur des Knorpels. Sitzungsber. der K. K. Akad. d. Wiss. in Wien., Bd. 57, 1868.

[2] "Das Verhältniss zwischen Protoplasma und Grundsubstanz im Thierkörper." Sitzungsber. d. K. K. Akad. d. Wien. Wien., Bd. 67, 1873, and *Wien. med. Jahrbücher*, 1873.

[3] Catalogue of the historical series in the museum of the Royal College of Surgeons, 1850, vol. i, p. 102.

[4] Disquisitiones microscopicæ de cartilaginibus in specie hyalinicis. Inaug.-Dissert., Dorpat, 1850.

[5] "Zur Anatomie und Histologie der Chimæra monstrosa." *Mueller's Archiv*, 1851, p. 242.

[6] "Ein Fall allgemeiner Ochronose der Knorpel und knorpelähnlichen Theile." *Virchow's Archiv*, xxxvii, 1866, p. 212.

[7] "Über Pigmentinfiltration des Knorpels." *Ibid.*, lxxii, 1878.

[8] Manuel d' histologie pathologique, Paris, 1869, p. 427.

[9] Lehrbuch der pathologischen Gewebelehre. Leipzig, 1878, p. 553.

[10] Sitzungsber. der K. K. Akademie d. Wiss. in Wien., Bd. 75, 1877.

seemed to point to their presence in man. Pigment particles were introduced into the circulation in the hope of discovering the manner in which they penetrate the tissue of cartilage, by Gerlach,[1] Maas,[2] Arnold,[3] and Nykamp and Treub[4]; Küttner, with the same end in view, introduced solutions into the trachea and examined the bronchial and tracheal cartilages[5]; and Hénoque,[6] Budge,[7] Tizzoni,[8] and others, forcibly injected liquids as well as solid particles into the tissues. The results of these experiments, and of examinations with various reagents, are contradictory of each other: For instance, while Bubnoff,[9] Hertwig,[10] Hénoque,[11] Loewe,[12] Thin,[13] Ewetzky,[14] Petrone,[15] Budge,[16] Nykamp,[17] Fürbringer,[18] and a number of others consider the existence of canals in the basis-substance of cartilage proved by their experiments and treatment of their preparations with silver nitrate, gold chloride, hyperosmic acid, chromic acid, ammonia bichro-

[1] Ueber das Verhalten des indigschwefelsauren Natrons im Knorpelgewebe lebender Thiere. Erlangen, 1876.

[2] "Ueber das Wachsthum und die Regeneration der Röhrenknochen." *Archiv für klinische Chirurgie*, xx, 1877.

[3] "Die Abscheidung des indigschwefelsauren Natron im Knorpelgewebe." *Virchow's Archiv*, lxxiii, 1878.

[4] "Beitrag zur Kenntniss der Structur des Knorpels." *Archiv für mikroskop. Anatomie*, xiv, 1877.

[5] "Die Abscheidung des indigschwefelsauren Natron in den Geweben der Lunge." *Centralblatt f. d. med. Wiss.*, 1875, No. 42, p. 268.

[6] "Structure des cartilages." *Gazette médicale*, 1873, p. 589; p. 617.

[7] "Die Saftbahnen im hyalinen Knorpel." *Archiv für mikroskop. Anatomie*, xiv, 1877; xvi, 1879.

[8] "Sulla istologica normale e patologica delle cartilagini ialini." *Archivio per le Scienze Mediche*, ii, 1877.

[9] *Loc. cit.*

[10] "Ueber die Entwickelung und den Bau des elastischen Gewebes im Netzknorpel." *Archiv für mikroskop. Anatomie*, ix, 1873, p. 80.

[11] *Loc. cit.*

[12] "Ueber eine eigenthümliche Zeichnung im Hyalinknorpel." *Wiener med. Jahrbücher*, 1874.

[13] "On the structure of hyaline cartilage." *Quarterly Journal of Microscopical Science*, vol. xvi, 1876.

[14] "Entzündungsversuche am Knorpel," Vorläufige Mittheilung, *Centralblatt f. d. med. Wiss.*, 1875, No. 16; Untersuchungen aus dem path.-anat. Institut zu Zürich, iii Heft, 1875.

[15] Sulla struttura normale e patologica delle cartilagine e degli epitelii. Napoli, 1876.

[16] *Loc. cit.*

[17] *Loc. cit.*

[18] "Ueber das Gewebe des Kopfknorpels der Cephalopoden." *Morpholog. Jahrbücher*, iii, 1877, p. 453.

mate, etc., etc., investigations by exactly the same means have convinced Sokolow,[1] Retzius,[2] Colomiatti,[3] Brückner,[4] Toldt,[5] Genzmer,[6] Gerlach,[7] Tillmanns,[8] Tizzoni,[9] and others, of just the contrary; and there is a third party which believes with Arnold[10] that the basis-substance is made up of fibrillæ, that there are delicate fissures between the fibrils, that these fissures penetrate the capsule, and that "the nutrient material passes through these interfibrillar and intracapsular fissures into the pericellular space." Flesch, the latest writer on the subject, adds[11] that these fissures need not necessarily be, and in fact are not, empty, but that they are occupied by the interfibrillar cement-substance, which, being of a "viscous-soft" (*zähweich*) material, permits the imbibition and conveyance of the nutrient liquid.

It is claimed that hyaline basis-substance consists of fine fibrils so closely held together by a cement-substance that the mass appears to be homogeneous. This idea, though not entirely novel, as the older anatomists seem to have had it,[12] has been brought forward by Tillmanns, and is doubtless original with him.[13] It is said that the interfibrillar cement-substance can be dissolved out by certain reagents and then

[1] Ueber den Bau des Nasenknorpels," etc., ref. Canstatt's Jahresbericht, 1870, p. 24.

[2] "Bitrag till Kännedomen um brusknäfnaden." *Nord. med. Arkiv.*, iv, 1872.

[3] "Sulla struttura delle cartilagini ialini e fibroelastica reticolata." *Gazetta Cliniche di Torino*, 1873, No. 32; *Rivista Clinica di Bologna*, 1874, No. 5; *Giornale della Acad. di Torino*, 1876.

[4] "Über Eiterbildung im hyalinen Knorpel." Inaug.-Dissert., Dorpat, 1873.

[5] Lehrbuch der Gewebelehre. Stuttgart, 1874, p. 143.

[6] "Ueber die Reaction des hyalinen Knorpels," etc. *Virchow's Archiv*, lxvii, 1875; *Centralblatt f. Chirurgie*, 1875, No. 146.

[7] *Loc. cit.*

[8] "Beiträge zur Histologie der Gelenke." *Archiv für mikroskop. Anatomie*, x, 1874, pp. 354, 435.

[9] *Loc. cit.*

[10] *Loc. cit.*

[11] Untersuchungen über die Grundsubstanz des hyalinen Knorpels. Würzburg: A. Stuber, 1880.

[12] See: Wm. Hunter "On the structure and diseases of articular cartilages," Philosoph. Transactions, vol. xlii, p. 514, London, 1742–43; M. de Làsone, "Second memoire sur l' organization des os," Mem. de l' Academie Roy. des Sciences, Tome 69, Paris, 1752; more recently also: Hoppe, *Virchow's Archiv*, v, p. 175.

[13] *Loc. cit.*, p. 401; and "Ueber die fibrilläre Structur des hyalinen Knorpels." *Archiv f. Anatomie u. Physiologie*, Anat. Abth., 1877, p. 9.

the fibrillation seen under the microscope. According to the varying arrangement and interrelation of the fibrillæ, Tillmanns speaks of three types of cartilage tissue, viz., parallel-fibery, netform, and lamellous. No doubt he saw under the microscope appearances which underlie the distinction which he thus made, but, unfortunately, he misinterpreted these appearances. Nevertheless, he has had followers. Thus Baber reported [1] that, having undertaken to test the accuracy of Tillmanns' assertions, and not succeeding in finding the fibrillation, although he had followed Tillmanns' method of maceration, he accidentally made momentary pressure on the glass cover, and thereupon obtained satisfactory proof of the fibrillar constitution of the basis-substance. Reeves [2] has also convinced himself of the existence of normal fibrillation in human cartilage. Ziegler seems to have done the same [3]; and Flesch regards it as a matter beyond question. He speaks of it as "generally known and most easily demonstrable." [4] Furthermore, he thinks that some portions, or perhaps layers, of the basis-substance are more compact than others, and that this may also account for the facility of cleavage in determinate directions.

Leidy insisted [5] that the basis-substance of hyaline cartilage has a peculiar filamentous structure, but his interpretation, that the granular filaments run simply parallel to each other, does not cover the truth and has not attracted any attention. With the exception of Leidy, however, no one, until nine years ago, seems to have questioned the homogeneousness of the mass of basis-substance in which the separate corpuscles were supposed to be imbedded. In 1872, Heitzmann [6] first proved the presence of a network structure in the basis-substance; one year later he discov-

[1] "On the structure of hyaline cartilage." *Journal of Anatomy and Physiology*, vol. x, part i, October, 1875.

[2] "On the structure of the matrix of human articular cartilage." *British Medical Journal*, Nov. 11, 1876, p. 616.

[3] Bericht der 50. Naturforsch. Versammlung zu München, 1877.

[4] *Loc. cit.*, p. 74.

[5] Proceedings of the Academy of Natural Sciences of Philadelphia, vol. iv, No. vi, 1848; and *American Journal of Medical Sciences*, April, 1849, p. 282.

[6] *Wiener Medizin. Jahrbücher*, Heft iv, 1872.

ered the structure of so-called protoplasm to be reticular, and claimed that both the reticulum of the protoplasm and that of the basis-substance are identical in nature; viz.: that both consist of the living matter proper. Heitzmann says that examination, by means of an immersion lens No. 10, of a thin section of fresh articular cartilage, placed in a one-half-per-cent. solution of common table-salt reveals details heretofore overlooked, viz.: The bodies of the cells appear finely granular, bounded by a somewhat denser layer. The contour of a cartilage cell being accurately in focus, there appears between it and the basis-substance a light, very narrow rim, which is traversed by numerous extremely delicate, radiating, grayish thorns or streaks. All these thorns are conical, the broad base emanating from the body of the cell and the thin point directed toward the basis-substance. Wherever two cells lie close together, the light rim between them is pierced by grayish threads. When in a cell the nucleus is distinctly seen, a narrow light rim is found to surround it, which on being sharply focused, also shows radiating thorns, the basis of which emanate from the nucleus and the points of which blend with the protoplasm of the cell. On carefully examining the basis-substance, a very delicate, as if granular, configuration is recognizable, dark fields alternating with light ones, and in some places the impression is given that the light fields form ramifications, or even a delicate network. Heitzmann also described and figured specimens stained with silver nitrate and gold chloride, and announced the following conclusions: viz.: "The bodies of cartilage cells have radiating offshoots. These offshoots form a delicate granular reticulum in the basis-substance. At the points of junction of hyaline cartilage with fibrous cartilage and with periosteum, the offshoots are very large and broad. They connect neighboring cells either directly or else indirectly through intervening delicate offshoots." Somewhat similar appearances had previously been more or less vaguely described, but not properly interpreted or appreciated, by Remak,[1]

[1] "Ueber die Entstehung des Bindegewebes und des Knorpels." *Archiv für Anatomie*, 1852, p. 63 *et seq.*

by Heidenhain,[1] by Broder,[2] by Fromann,[3] and possibly by others.

After Heitzmann, Hertwig[4] observed processes of living matter penetrate the basis-substance of reticular cartilage; and Colomiatti stated[5] that he had repeated the investigations of Heitzmann, but had failed to find cell offshoots in hyaline cartilage either after treatment with gold or silver or *in vivo*, although he had seen cartilage-cell offshoots in other than hyaline cartilage.

I have had the opportunity to repeat Heitzmann's investigations under his own eye and with his assistance, but the results as to their correctness at which I arrived, were, to the best of my belief, uninfluenced by him. I reported in 1875[6] that I had seen the network structure in the corpuscles of hyaline cartilage, in the nucleus and in the basis-substance, exactly as Heitzmann had described it two years previously.[7] "If the nucleus of the cartilage corpuscle be visible, it appears either homogeneous or composed of a dense meshwork of living matter. From its periphery proceed fine conical thorns, which lead to a meshwork pervading the whole corpuscle, the threads of which form, at the point of intersection, thickenings, granules, or small clumps of living matter. In the lighter-looking narrow seam, existing between the corpuscles and the surrounding matrix, we may also recognize fine threads which go from the periphery of the corpuscle and are lost to the view in the matrix. On examining such a fresh preparation upon the heated stage, we recognize, at a temperature of 86° to 95° F., a continual but very slow change in the living matter of those cartilage corpuscles which distinctly show the network; the points of intersection of threads move nearer

[1] *Loc. cit.*

[2] Ein Beitrag zur Histologie des Knorpels. Dissert., Zürich, 1865.

[3] Untersuchungen über die normale und pathologische Anatomie des Rückenmarkes. II Theil. Jena, 1867, pp. 29, 30.

[4] *Loc. cit.* [5] *Loc. cit.*

[6] Transactions of the American Medical Association, vol. xxvi, 1875, pp. 163 and 164.

[7] Untersuchungen über das Protoplasma. II. Das Verhältniss zwischen Protoplasma und Grundsubstanz im Thierkörper. Sitzungber. d. K. K. Akad. d. Wiss. in Wien, lxvii, May, 1873.

together or go further apart ; sometimes a few granules lying close to each other unite into one little lump, so that the threads between them disappear, then the latter reappear, lengthen and shorten ; and this change in the form of the interior network continues for some little time, and without any perceptible influence upon the form of the corpuscle as a whole.

"Careful examination of the matrix reveals throughout its whole extent the existence of a very delicate, more or less distinct network of living matter ; and in many instances the connection of the threads proceeding from the corpuscles with this delicate network can be traced.

"To show the structure of both the cartilage corpuscles and the matrix still more plainly, we may resort to the method of tinction of preparations by nitrate of silver and chloride of gold, as well as the examination of cartilage during normal calcification, and in its inflamed conditions.

"It is well known that chloride of gold stains living matter dark violet, while nitrate of silver acts upon the matrix, and by darkening it, makes the living matter appear of a light color or colorless. The appearances obtained thus complement each other ; and the network proceeding from the corpuscles and ramifying all through the matrix, is seen, with the same magnifying power, as constituted by violet threads and granules in the first case, and by white processes or empty spaces in the second case. [Drawings illustrating both these appearances accompany my article in the American Transactions.] As the deposition of lime salts takes place only in the matrix, the living matter itself remaining free, careful examination during such depositions, especially in cases of artificially produced inflammation, also brings to view the fine network of living matter traversing the matrix."

In January, 1876, Thin's memoir was published,[1] in which he reported that, in particular preparations, he had seen "fine glistening fibres enter the cartilage substance, into which, however, he has not been able to follow them." Again : "The ordinary granular protoplasmic cells of hyaline carti-

[1] It is dated August, 1875. *loc. cit.*

lage are analogous, according to the views of the author, to the stellate cells of the cornea and connective tissue generally." Thin obtained by silver staining appearances similar to Heitzmann's, but unfortunately misinterpreted them. He says: "Heitzmann believes that the appearances which he has reproduced are those of a cell and its protoplasmic processes. The author interprets the appearances shown in Heitzmann's own drawings as representing stellate spaces, and sees nothing in them that he can interpret as cell processes; being thus at one with him as regards the fact observed, but differing from him in regard to its interpretation." [1]

In 1879 Spina reviewed the subject.[2] He accorded to Heitzmann the merit of the discovery, but as in the intervening seven years I alone had publicly corroborated it, and he was not aware of that corroboration, he thought that "the existence of cells with solid offshoots in genuine hyaline cartilage is not definitely proved," and undertook to settle the question. After many fruitless attempts he found out a method of examination "by which ramifying cells in hyaline cartilage can be demonstrated not only with ease, but also with certainty." The method and the results, as he has described them, are as follows: "The cartilage, best the articular ends of bones, is placed into alcohol for three or four days; then the sections are made and the examination is conducted in alcohol. From such specimens positive proof is obtained that the cells of hyaline cartilage have solid offshoots. These offshoots emanate mostly from the body of the shrivelled cells, penetrate the basis-substance, and inosculate with offshoots of other cells. Their number and thickness are subject to numerous variations. * * * The cell offshoots do not, as a rule, ramify. * * * Examination with powerful immersion lenses (Hartnack, No. 15) teaches positively that the cell offshoots not only pierce the capsule, but that the capsule extends also to the offshoots themselves, so that at their origin they are surrounded like the cell body by a wall. * * * Upon adding a drop of

[1] *Loc. cit.*, p. 22.

[2] "Ueber die Saftbahnen des hyalinen Knorpels." Sitzungsber. der K. K. Akad. d. Wiss. in Wien, lxxx, Abth. iii, Nov., 1879.

glycerine to the alcohol specimen, or on staining it after one of the usual methods, the cell offshoots disappear more or less rapidly; hence, it is clear that the hyaline, structureless aspect of the cartilage basis-substance, is really due to the methods of preparation hitherto in use, while, when examined in alcohol, as above described, the cell offshoots invariably become visible." He added that he has succeeded a few times in seeing—faintly only, it is true—the same structure in living hyaline cartilages. On incorporating, for a sufficient length of time, carmine into the body of frogs, Spina found cartilage corpuscles of which the nuclei, the body, and the offshoots had taken in some of the coloring matter. As the offshoots disappeared and the carmine granules seemed to lie in the hyaline basis-substance when a drop of glycerine was added, it is easy to see how previous investigators came to be misled into supposing the coloring matter to have passed into the hyaline substance, and into interfibrillar fissures. With excessive caution, Spina adds: "Whether they (the coloring particles) can also move along outside of the cell offshoots has not yet been proved."

In the same year Prudden,[1] and, in 1880, Flesch,[2] also described cilia-like processes of cartilage corpuscles; and the latter admitted that in exceptional cases he had succeeded in tracing them more or less distinctly into the basis-substance.

Section II.—*Personal Investigation.*

I. Having, as already detailed, familiarized myself with the investigation of cartilage tissue, I entered upon the examination of the laryngeal cartilages. Of the many specimens examined, I shall now describe a few of the thyroid. Longitudinal sections through the lateral plates of the thyroid cartilage of a man of about 25 years, hardened in chromic acid and stained with an ammoniacal carmine solution, exhibit with low powers of the microscope (150 to 200

[1] "Beobachtungen am lebenden Knorpel." *Virchow's Archiv*, lxxv, 1879, p. 185.

[2] *Loc. cit.*, pp. 59–63.

diam.) the following: The cartilage corpuscles, either single, in pairs, or in groups of from three to six, or even more, are imbedded in a basis-substance which, for the most part, is homogeneous-looking or indistinctly granular, but in some portions finely striated. The homogeneous or indistinctly granular-looking basis-substance is that which bears the name hyaline basis-substance; the striated is termed fibrous, although actual fibrillæ appear only on the edges of the specimen, or when the tissue is torn and mutilated. The fibrous basis-substance is intermixed, without any regularity, with the hyaline, and usually sharply separated from it. Not infrequently a number of cartilage corpuscles, or groups of cartilage corpuscles, are surrounded by fibrous basis-substance, the striations of which run, as a rule, in a sagittal direction, *i.e.*, vertical to the surface. Within the fibrous basis-substance the cartilage corpuscles are at most points sparsely scattered or absent; here and there, however, they are more numerous, in rows or elongated, corresponding to the direction of the striations. It also occurs that striated portions of the basis-substance contain very minute globular or oblong corpuscles, sometimes to such an extent that the striated structure is concealed by the large number of these corpuscles.

Fig. 1 exhibits the appearance of the constituent parts, with an amplification of 100 diam. The fibrous portion is seen to occupy the centre of a longitudinal section of one of the plates of the thyroid cartilage. This is not regularly the case in every cut, and was exceptionally well marked in the section from which the drawing was made. In some sections the fibrous cartilage is altogether absent, but every laryngeal cartilage contains some fibrous mixed with hyaline portions. *A*, perichondrium toward the mucous membrane. *B*, perichondrium toward the skin. *F*, fibrous portion of cartilage. *H*, hyaline portion of cartilage.

Under higher magnifying powers (500 to 600 diam.) single cartilage corpuscles exhibit features, frequently before described, with coarsely granular nuclei. Around the nucleus finer granules are visible. At the periphery of the cartilage corpuscle there are several strata of higher refracting power, especially the zone nearest the basis-substance, which, as a

rule, appears very shining and is what is termed the capsule of the cartilage corpuscle. Not infrequently the cartilage corpuscle is very indistinct, being but slightly more granular than the surrounding basis-substance; then almost nothing but the nucleus marks its presence and its place. In twin formations of cartilage corpuscles, which are often met with, the zone of division between the two corpuscles is identical with that surrounding both, in the shape of a capsule. Of the same nature are the zones of division that are seen in clusters of cartilage corpuscles.

The so-called hyaline basis-substance throughout its whole extent now appears finely granular; as a rule, the granulation is more distinct midway between the corpuscles than in their immediate vicinity. The fibrous portions of the basis-substance are seen to be made up of extremely minute spindles, which, by being grouped longitudinally, produce the aspect of striation. The spindles or fibres are separated from each other by light rims, and both the spindles and the rims look finely granular. Between the spindles may often be seen small globular bodies, sometimes scattered, sometimes in clusters, of which the size and shape greatly vary, reaching occasionally the size and shape of a regular cartilage corpuscle. In some striated fields blood-vessels, both arterial and capillary, can be seen; the former with the characteristic muscle-coat, the latter with the endothelial wall, besides holding red blood corpuscles in their calibres.

Fig. 2, representing the fibrous portion of thyroid cartilage amplified 600 diam., shows *C*, a cartilage corpuscle surrounded by a dense basis-substance; *G*, granules of living matter in a dense fibrous structure; *B*, a capillary blood-vessel; and *V*, a small vein.

The highest powers of the microscope (1000 to 1200 diam.) reveal the reticular structure of cartilage corpuscles, as it is known since 1873. All granules within the nucleus and all granules within the corpuscle are uninterruptedly connected by delicate threads. The intranuclear network is connected with the corpuscular reticulum by radiating conical spokes traversing the light rim around the nucleus;

and, at the periphery of the corpuscle, similar conical spokes pierce a narrow light rim and enter the basis-substance, in which, especially in the highly refracting zone, termed capsule, they are usually lost to sight. Cartilage corpuscles even which have become so pale as to leave only a dim trace of their former contour visible, still exhibit more or less distinct traces of the reticular structure.

The same structure may be seen throughout the so-called hyaline basis-substance—more distinct in the middle of the space between the corpuscles than immediately around the corpuscles themselves. The fibrous portion of the basis-substance has also a reticular structure. The bodies of the slender spindles show a network without the application of any reagent, and the light rims between the spindles are traversed by delicate threads running in a vertical direction to the longitudinal diameter of the spindles. All granules and lumps scattered through the fibrous basis-substance are surrounded by light rims, which are pierced by conical spokes inosculating with the reticulum of the neighboring spindles.

The reticular structure of cartilage corpuscles, *C C*, twin-formations; the indistinct reticulum in hyaline basis-substance, *B*; and a number of small granules of living matter in fibrous basis-substance, *F*, the spindles and granules being connected by fine threads, are exhibited in fig. 3 which represents a sagittal section of the thyroid cartilage of an adult amplified 1200 diam.

I have treated sections of the same cartilage after they had for several days been washed out with distilled water, with a one-half-per-cent. solution of gold chloride, whereupon they assumed a dark purple color, and showed all the features described, somewhat more distinctly than simple carmine preparations. I deem their detailed description unnecessary.

II. When I became acquainted with Spina's researches, cited in my historical sketch, I deemed it of importance to repeat the examination according to his method. I therefore placed a larynx immediately after removal from the body of a girl, aged 24 years, into strong alcohol, and after four days made thin sections from the thyroid cartilage in

a horizontal direction, transferred them in alcohol to the slide, and examined them with both low and high powers, adding from time to time a drop of strong alcohol to prevent the specimen from drying. The appearance presented by such a specimen is truly surprising. As a matter of course, the cartilage corpuscles are shrivelled up so that more or less space is left between their jagged periphery and the border of the basis-substance. With an amplification of 500 diam., the basis-substance is seen pierced by light filaments, which, in many instances, can be traced through the intervening space into the body of the cartilage corpuscle. Most of these filaments radiate around the corpuscle, and immediately after penetrating the basis-substance, diverge and form a reticulum throughout its extent. Cartilage corpuscles located near each other, are directly connected by non-ramifying and occasionally by ramifying offshoots, or by bundles of such offshoots of a more or less parallel course. The reticulum in the basis substance is either radiating or irregularly arranged around the corpuscle. Contrary to the assertion of Spina, the filaments or offshoots do, as a rule, ramify, except those that directly connect the neighboring corpuscles. Sometimes thick bundles of offshoots emanate from opposite poles of the corpuscles, while intervening portions of the periphery are almost devoid of offshoots. Toward the periphery of the thyroid cartilage, —where, as is well known, the cartilage corpuscles elongate, becoming smaller and spindle-shaped and more or less parallel to each other,—the offshoots are given off rectangularly to the axis of the corpuscles.

High magnifying powers, immersion lenses No. 10 and No. 12, conclusively prove the connection of the offshoots with the cartilage corpuscles. Portions of the basis-substance which, with lower powers, looked only granular, now show a delicate reticulum, which, even when coarser offshoots are wanting, is connected with the cartilage corpuscle through delicate, and more or less conical, offshoots from the surface of the corpuscle.

The light interstices between the fibres of striated basis-substance, are also traversed by delicate grayish thorns.

Such thorns are visible even in the perichondrium. Through the fibrous bundles of the perichondrium run in a nearly rectangular direction, delicate light streaks, while the interstices between the bundles and the spaces left between the corpuscular elements and the bundles, exhibit delicate conical grayish threads, the direction of which corresponds to these light streaks.

The highest powers of the microscope disclosed in one of the specimens examined another feature in the hyaline basis-substance, viz., the presence of a number of granules or minute lumps of varying shape, some interwoven with the direct offshoots of the corpuscles, and some with the threads forming the finer network of the basis-substance. They appeared to be thickened points of intersection, knots or nodes, composed of the same material as the offshoots and threads themselves. They were unquestionably granules of living matter. I found their greatest development in a case examined without Spina's method, a case which I shall describe presently. Fig. 4 shows a horizontal section of a thyroid cartilage, which was hardened in alcohol and examined by the method of Spina, with an amplification of 1200 diam. *C*, shrivelled cartilage corpuscle; *O*, longitudinal offshoots connecting cartilage corpuscles; *R*, reticulum in the hyaline basis-substance; *G*, granules of living matter, which are seen to be part and parcel of the reticulum.

III. The observation which I am now about to record, was made in specimens of the thyroid cartilage removed from the body of a rather stout man, 48 years old. After having been hardened in chromic acid solution, without any other reagent, they exhibited formations in the basis-substance which, so far as I am aware, have never before been described. I have alluded to them as found in one of the specimens examined, with the highest powers of the microscope, by the alcohol method of Spina. These formations are shown in fig. 5, with an amplification of 600, and in fig. 6, with an amplification of 1200 diameters.

As to the cartilage corpuscles in these specimens, many of them were larger and more coarsely granular than are commonly observed: otherwise, their characters and the arrange-

ments of the basis-substance, both so-called hyaline and fibrous, were like those described before. The intranuclear, intracorpuscular, and intercorpuscular networks were with high powers well shown.

The very remarkable feature was that with quite low power the basis-substance was seen to be speckled and studded with granules or lumps varying from that of a point at the limit of the visible to that approaching the dimensions of a regular cartilage corpuscle. Of course, no one must for a moment think of any thing like the pathological conditions that have been described either as granular degenerations of the cartilage basis-substance, or as incrustations of the corpuscles. Not only were the appearances entirely different and the cartilage healthy—as otherwise ascertainable as well as from the known condition of the man and of the cause of his death—but the true nature of the lumps was made perfectly clear by examination with higher powers.

When magnified to the extent of 600 diameters, the same relative appearance was preserved. The lumps in the basis-substance still varied in size from the limit of the visible to the magnitude of ordinary cartilage corpuscles; but in all the larger lumps, differentiations were visible which approached them in structure as well as in size to cartilage corpuscles. In some, one or more vacuoles, in others, a small or large nucleus, or even two nuclei, could be made out; and a few (*i. e.*, occasionally one in some fields) showed irregular twin, or even triplet formation.

The highest power threw a wonderful light upon these lumps. They were seen to be masses of living matter. The larger showed a network in their interior, some without and some with a nucleus, and the latter, when present, was sometimes homogeneous and sometimes reticulated. All the lumps, except the smaller, were surrounded by a distinct light seam, through which radiating conical offshoots passed to the network in the basis-substance; and all of them, even the smallest, sent delicate offshoots connecting them with that network, or were themselves part and parcel (*i. e.*, thickened points of intersection of the threads) of that network.

After having studied such a specimen, it was easy to interpret correctly the intrareticular granules seen in the alcohol specimen represented in fig. 4.

Fig. 5 shows a horizontal section of the thyroid cartilage of a robust, rather stout man, 48 years old, amplified 600 diam. *C C*, cartilage corpuscles; *G*, granules or lumps scattered through the hyaline basis-substance; *F*, fibrous portion of cartilage.

Fig. 6 shows a field of the same specimen with an amplification of 1200 diam. *C*, cartilage corpuscle with distinct reticular structure surrounded by a dense basis-substance, the so-called capsule; *B*, hyaline basis-substance with faint reticular structure; *G*, granules or lumps scattered through the hyaline basis-substance, connected with its reticulum.

Section III.—*Deductive.**

I.—Regarding the essential structure.

Instead of being a mass of basis-substance in which a number of cartilage corpuscles are imbedded, hyaline cartilage is a filigree of living matter, in the meshes of which lumps of basis-substance are imbedded.

The difference between the former and the present view of the essential structure is a radical one. Of its full import I shall say more before the end of this Section.

The number of investigators who have hitherto succeeded in observing cartilage corpuscles sending offshoots into the basis-substance, is very small; the number of those who have succeeded in tracing such offshoots far enough into the basis-substance to observe their forming a network is smaller still. As a rule, this network can be seen only very faintly in fresh specimens, and in specimens obtained either after hardening in chromic acid solution or by other methods; but the staining with gold chloride, as practised by Heitzmann in 1872 brought it more plainly into view, as did also the alcohol method of examination devised by Spina in 1879. The fact that in the intervening seven years many observers have endeavored to see it and failed,

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may be due, as claimed by Spina, to the method employed. I certainly accord great merit to Spina for his discovery of the effect of the alcohol treatment. Not only is it far simpler in every way than the gold-chloride treatment, but being very easy of employment it is also invariably, so far as my experience hitherto has gone, attended with success. Although many have failed with former methods, I venture to say that no one who follows the directions given by Spina, but will see the offshoots and the network. A different question, however, than the mere seeing, is the correct interpretation. Spina himself does not follow out the logical consequences of his observations, and Flesch, the author of the latest publication on the subject, goes only so far as to say "the offshoots are lost in the basis-substance, their continuation forms the cement-substance."[1] Perhaps it needed the occurrence of so convincing a case as that recorded in the present paper to place the matter of interpretation beyond dispute. At all events, so far as I am aware, no such clear demonstration of the correct interpretation of the structure of cartilage was ever had before. It is the case which figs. 5 and 6 illustrate. The basis-substance is crowded with lumps visible with even low powers of the microscope without any other reagent than that the larynx had been preserved in chromic acid solution. The lumps are proved to be living matter by all the tests applied to them. Their identity in this respect and uninterrupted filamentous and granular connection with the cartilage corpuscles on the one hand and with the granules and threads of the intercorpuscular network on the other, render doubt as to the interpretation impossible. In other words, we have in hyaline cartilage before us a mass of living matter arranged principally in the form of a granular network with large and small meshes; the large meshes contain chondrogenous firm basis-substance, the small meshes contain liquid, and with their usual but perhaps not essential limiting layer constitute the cartilage corpuscles; thickened points of intersection of the filaments of the

[1] *Loc. cit.*, p. 85. Though published in 1880, Flesch tells us that his work was finished by the end of 1878. Spina's communication is not referred to. Flesch employed gold chloride and other methods.

network constitute granules; comparatively smaller and larger lumps of living matter exist 1) in the corpuscle as nucleoli and nuclei, the latter also usually already reticulated, and 2) in the basis-substance as granules and small corpuscles.

II.—Regarding the so-called "juice routes" or "lymph-channels."

In my historical sketch I have given a very slight idea only of the many and elaborate researches to explain how nutrient juice might reach the cartilage corpuscle, isolated and enclosed in the hard basis-substance. But the truth being that the corpuscle is not isolated and so enclosed, much of the laborious investigation and ingenious reasoning was inapplicable to the case. Of course I do not agree with those who think that cartilage contains a system of tubular or other-shaped channels, either with or without a lining membrane, or that it contains fibrils with interfibrillar cement-substance; *i. e.*, I do not agree with the advocates of either of these views in the sense in which they hold them. But I can see how, in the absence of the guiding knowledge which was supplied by Heitzmann's great discovery of the arrangement of living matter, these different investigators arrived at their conclusions. The minute blocks of basis-substance are separated from each other, and at the same time joined together, by the living matter between them. This is the ground for the interpretation, on the one hand, that there exists a "viscous-soft" cement-substance in the intercorpuscular space capable of conveying juices, and, on the other, that there are canals which hold offshoots of the corpuscles. There is no good reason that I know of, for denying that, in addition to the living matter, a certain amount of liquid may be circulating in such canals, *i. e.*, in the interstices between blocks of basis-substance in the intercorpuscular spaces (and perhaps also around the corpuscles themselves), and that such liquid may carry particles of foreign bodies as charcoal, carmine, cinnabar, etc., far into the cartilaginous tissue; but the liquid is not the essential portion of the contents of these canals, and if experimenters have succeeded in injecting them, the high

pressure exerted upon the cartilage must have pushed aside or compressed the living matter. What the "juice routes" are, is clear enough. When Spina had demonstrated that coloring matter is absorbed into cartilaginous tissue by means of the offshoots of the cartilage corpuscles, he need not have added the remark that proof is wanting that the coloring matter can pass through cartilage outside of such offshoots. Such proof will ever remain wanting. Every cartilage corpuscle, no matter how far removed it be from the source of nutrient supply, is more or less directly connected therewith by means of the filigree of living matter; and this filigree itself constitutes the system of juice routes.

III.—Regarding the intermixture of fibrous basis-substance.

The laryngeal, as well as the tracheal and the costal cartilages, invariably contain, irregularly intermixed with hyaline basis-substance, a number of small or large portions of striated or fibrous basis-substance. Now, notwithstanding the constancy of this occurrence, all authors on the subject describe it as the result either of a degenerative process (Rheiner, Luschka, Schottelius, etc.), or of atrophy (Rokitanski, etc.). According to Schottelius,[1] the process commences in about the tenth or twelfth year of life, and immediately introduces profound destructions of the tissue. He says that the fibres are cylindrical filaments, arranged in general in a parallel direction, but somewhat interlaced. It seems to him that the formation of these fibres occurs when, in a degenerated basis-substance, the cartilage corpuscles perish; perhaps by a coagulation process similar to that by which fibrine is formed. I shall show in the next chapter that Schottelius is mistaken in believing that the intermixture of striated basis-substance is not found until the approach of puberty. But even were he right, I should still contend that I have met with fibrous basis-substance in healthy as well as in diseased hyaline cartilage, and that investigation has not led me to believe that its presence

[1] Die Kehlkopfknorpel. Untersuchungen über deren physiologische und pathologische Texturveränderungen. Wiesbaden, J. F. Bergmann, 1879, pp. 20, 21.

necessarily results from a degenerative process. When, *f. i.*, I find it in every healthy thyroid cartilage that I examine, I cannot but regard its development as normal. Is it not supererogation to look upon a phenomenon as degeneration which is present—as is this, at least so far as my experience goes—in every individual, without exception? I think the presence of fibrous portions must be considered normal in cartilages that appear healthy in every other respect; but I do not mean to deny the possibility of fibrous degeneration with other pathological conditions. In such a case of transformation there must be an intermediate state. All recent researches tend more and more to show that one tissue is never directly changed into another, and I cannot easily believe that what is first a hyaline basis-substance can directly become a fibrous one. Attempts to explain any such direct transformation have proved failures, I believe; and even with our present knowledge of the existence of living matter within the basis-substance, it would be a difficult task to realize that the firm, solid, chondrogenous basis-substance can assume the striated form. The least that would have to be admitted is a melting, *i. e.*, a solution or softening of the basis-substance in certain territories of hyaline cartilage, with accompanying fusion of the living matter, and subsequent splitting up of the mass or masses of the latter into delicate spindles.

That striated portions of hyaline cartilage have in the course of normal development arisen from medullary tissue, present in the fœtal condition, seems far more probable. If this view be adopted, we need not assume with Schottelius and others, that all the blood-vessels found after puberty are necessarily newly formed, but that some have been preserved from the infantile state. Indeed, I have met with appearances in my specimens which seemed strongly to indicate that some of the blood-vessels formerly present in the medullary tissue are now present between the fibres, while others have become obliterated, solidified, and transformed into the basis-substance themselves.

IV.—Regarding the cell-doctrine and the bioplasson-doctrine.

Just as the study of cartilage led to the cell-doctrine, which at the time of its establishment was a great advance in biological science, so the further study of cartilage supplied the basis for a generalization which is a further development, and must take the place, of the cell-doctrine. This is Heitzmann's doctrine of living matter, or, as I have named it, the *bioplasson-doctrine*.[1]

When the term "cell" was introduced, by Schleiden and Schwann, into histology, it was believed that the body on ultimate morphological analysis was found to consist of a number of minute vesicles or sacs, enclosing liquid contents in which is suspended a more solid body, the nucleus (this latter frequently containing a smaller similar body, the nucleolus, and this sometimes a still smaller one, the nucleolinus). For fully twenty years this idea has been known to be erroneous. Indeed, Goodsir nearly forty years ago—only a few years after Schwann had established the cell-doctrine and attributed the so-called metabolic or vital power to the cell-membrane—had experimentally determined that the seat of the vital process of secretion is not in the vesicle as such, but in the so-called cell-contents; Naegeli, in 1845, and Alexander Braun, in 1851, had also shown the cell-wall to be comparatively unimportant; and in 1857 Leydig had declared the "cell" to consist only of a soft substance enclosing a nucleus. Certainly, twenty years ago it was proved beyond dispute by Max Schultze, Beale, Hæckel, and others, that what was called a "cell" was not a vesicle, but essentially a jelly-like lump of living matter characterized by the presence of a nucleus; soon after, Robin, Brücke, Kühne, Stricker, and others, conclusively showed that not even a nucleus is an essential constituent of an elementary organism; and biologists were compelled to transfer the power of manifesting vital properties to "living matter" instead of restricting this power to any definite form or element. As long ago as in 1861, Brücke proposed to discontinue the use of the word "cell" as being a misnomer and misleading, and offered as a substitute the expression "elementary or-

[1] "Notice of the Bioplasson-Doctrine." *Transactions of the American Medical Association*, vol. xxvi, 1875.

ganism." Beale proposed, instead, the term "bioplast" to designate any definite mass of living matter, and Hæckel the term "plastid."[1] From the latter I devised the word "plastidule" as synonymous with ultimate molecule of the substance of living matter.[2] Elementary living matter is called with Dujardin "sarcode," or with Von Mohl "protoplasm," or with Beale "bioplasm," or, still better (because it is a designation etymologically more nearly meaning living, forming matter), "bioplasson."[3] Of these four synonymous terms, protoplasm is best known, but has been used in other senses than to designate merely elementary living matter. I, therefore, think that bioplasson is to be preferred.

According to Drysdale,[4] Dr. John Fletcher of Edinburgh was the first[5] who clearly abandoned the idea that the material elements of an organism require the addition "of an immaterial or spiritual essence, substance, or power, general or local, whose presence is the efficient cause of life," and who arrived at the conclusion that "it is only in virtue of a specially living matter, universally diffused and intimately interwoven with its texture, that any tissue or part possesses vitality." He denied vitality to any gaseous or purely liquid fluid, and any hard or rigid solid; and thought the only truly living matter consisted "of the gray matter of the ganglionic nerves, which he held to be universally

[1] The term "Plastid" was intended by Hæckel to include every form-element, whether a cell in the older sense or a lump of living matter without an investing membrane, and whether nucleated or unnucleated. For the nucleated plastid he retained the word cell or cyte, the unnucleated he called cell-like or cytode; and, according to his precise discrimination, there are therefore four kinds of plastids, viz.: 1. Gymnocytodes, or nude cytodes, *i.e.*, unnucleated lumps of living matter without membrane; 2. Lepocytodes, or covered cytodes, *i. e.*, unnucleated plastids with investing membrane; 3. Gymnocytes, or nude cells, *i. e.*, nucleated plastids without investing membrane; 4. Lepocytes, or covered cells, *i. e.*, cells with a cell-wall. The progress of histology has made these distinctions for that department of less value than they were when originally made, but they are still very useful for natural history purposes.

[2] See *London Monthly Microscopical Journal*, 1872, p. 182; "Proceedings American Association for the Advancement of Science," 1874; and "On the Plastidule Hypothesis," Proceedings of the same, 1876.

[3] Of course, dead bioplasson is a contradiction in terms: bioplasson deprived of vitality is no longer bioplasson at all, but merely the chemical remains of what once was bioplasson. If this be remembered there will be no confusion, even if the word be used in describing tissues, etc., after death.

[4] The Protoplasmic Theory of Life, London, 1874.

[5] Rudiments of Physiology, Edinburgh, 1835.

diffused, and the gray matter of the brain and spinal marrow." He described it as a "nitrogenous, pulpy, translucent, homogeneous matter, yielding, after death, fibrin." "Chemical analysis, accordingly, must be considered as useful in showing us, not what such matter *was composed of* while it possessed vitality, but what it is composed of *afterward*." "Not only is every vital action traced to molecular change, and to consumption and regeneration of this structureless, semi-fluid matter, combined in a way entirely *sui generis*, but the initiation of these changes is brought by Fletcher into absolute dependence on stimuli, and all spontaneity or autonomy is denied to matter in the living just as in the dead state."

As Fletcher's work was published in 1835, several years before even the establishment of the cell-doctrine, we cannot but agree so far with Drysdale as to say that Fletcher has framed "a hypothesis of the anatomical nature of the living matter which anticipates in a remarkable manner" its discovery! In 1850, Cohn[1] recognized the protoplasm "as the contractile element, and as what gives to the zoöspore the faculty of altering its figure without any corresponding change in volume." He concludes that protoplasm "must be regarded as the prime seat of almost all vital activity, but especially of all the motile phenomena in the interior of the cell." In 1853 Huxley[2] said "vitality, the faculty, that is, of exhibiting definite cycles of change in form and composition, is a property inherent in certain kinds of matter." In 1855 Unger[3] thought that "the proximate cause of the movements of the sap in the cells is to be sought neither in diosmosis, nor in the action of the nuclear vesicle, nor in any mechanical contrivance, such as cilia, but it lies rather in the constitution of the self-moving protoplasm, which, as an especially nitrogenous body of the nature of that simple contractile animal substance called sarcode, produces the rhythmically advancing contraction and expansion."

[1] "Nachträge zur Naturgeschichte des Protococcus pluvialis." *Nova acta Acad. Leop.-Carol.*, vol. xxii, part i., p. 605.

[2] "Review of the Cell-theory." *British and Foreign Medico-chirurg. Review*, Oct., 1853.

[3] Anatomie und Physiologie der Pflanzen, 1855, pp. 280, 282.

In 1856 Lord S. G. Osborne discovered carmine staining, and distinguished by means of coloring it the living formative matter from the formed material, a means which has borne important fruits in the discovery of Cohnheim's staining of living matter by gold chloride, and in that of Recklinghausen's staining all except living matter by silver nitrate.

In 1858, and in a number of later articles,[1] Max Schultze, by showing that, as had been hypothetically supposed by Unger, the movements of the pseudopodia and the granules are really produced by active contractile movements of the protoplasm, and by other observations, contributed much to the establishment of the theory of living matter. Hæckel has also for many years, and in various publications,[2] labored to maintain and extend the same theory, of which he thus expresses himself.[3] "The protoplasm or sarcode theory, that is * * * that this albuminous material is the original active substratum of all vital phenomena may, perhaps, be considered one of the greatest achievements of modern biology, and one of the richest in results." And says Drysdale[4]: "If the grand theory of the one true living matter was, as we have seen, hypothetically advanced by Fletcher, yet the merit of the discovery of the actual anatomical representation of it belongs to Beale, in accordance with the usual and right award of the title of discoverer to him alone who demonstrates truths by proof and fact. * * * The cardinal point in the theory of Dr. Beale is not the destruction of the completeness of the cell of Schwann as the elementary unit, for that was already accomplished by others. * * * But that, from the earliest visible speck of germ, up to the last moment of

[1] "Ueber innere Bewegungs-Erscheinungen bei Diatomeen," *Müller's Archiv*, 1858, p. 330; "Ueber Cornuspira," *Archiv f. Naturgesch.*, 1860, p. 287; "Ueber Muskelkörperchen und das was man eine Zelle zu nennen habe," *Reichert und Du Bois-Reymond's Archiv*, 1861, p. 1; Das Protoplasma der Rhizopoden und der Pflanzenzellen, Leipzig, 1863.

[2] Monographie der Radiolarien, 1862, pp. 89, 116; "Ueber den Sarcodekörper der Rhizopoden," *Zeitsch. f. Wissensch. Zoölogie*, 1865, p. 342; Generelle Morphologie, vol. i, pp. 269, 289.

[3] Monographie der Moneren," *Jenaische Zeitschft. f. Medicin und Naturwissenschaft*, 1868, iv, 1; translation in *Quarterly Journal of Microscopical Science*, London, 1869, vol. ix, p. 223.

[4] *Loc. cit.*, p. 42, *et seq.*

life, in every living thing, plant, animal, and protist, the attribute of life is restricted to one anatomical element alone, and this homogeneous and structureless; while all the rest of the infinite variety of structure and composition, solid and fluid, which make up living beings, is merely passive and lifeless formed material. This distinction into only two radically different kinds of matter, viz., the living or germinal matter and the formed material, gives the clue whereby he clears up the confusion into which the cell-doctrine had fallen, and gives the point of departure for the theory of innate independent life of each part, which the cell-theory had aimed at but failed to make good. The one true and only living matter—called by Beale germinal matter, or bioplasm— is described as 'always transparent and colorless, and, as far as can be ascertained by examination with the highest powers, perfectly structureless; and it exhibits those same characters at every period of its existence.' * * * The living matter of Beale corresponds to the following histological elements of other authors: The viscid nitrogenous substance within the primordial utricle, called by Von Mohl protoplasm; the primordial utricle itself, in Naegeli's sense of that term, viz., the layer of protoplasm next the cell-wall; the transparent, semi-fluid matter occupying the spaces and intervals between the threads and walls of those spaces formed by the so-called vacuolation of protoplasmic masses; the greater part of the sarcode of the monera, rhizopoda, and other low organisms; the white blood-corpuscles, pus-corpuscles, and other naked wandering masses of living matter; the so-called nucleus of the secreting cells, and of the tissues of the higher animals, and many plant-cells; the nuclei of the cells of the gray matter of the brain, spinal marrow, and ganglions, and the nuclei of nerve-fibres. The term of true living or germinal matter can never be given to the following parts, although to some of them the word protoplasm has been erroneously applied, viz., the cell-wall of plants or animals, however delicate or gelatinous; the threads or filaments and walls of the vacuoles within protoplasmic masses or cells; the wall of the primordial utricle; the true fibrous, connective, elastic, bony, or other

tissues generally included among the living parts of animals; even the proper contractile fibre of the muscles, the radiating fibres of the caudate nerve-cells, and the outer coat of those cells, besides the nerve-fibres in general; the hard parts of epithelial cells, and all liquid secretions; the cilia; the tissue of cuticle, hair, nails, horn, and all analogous parts in plants; the granules in sarcode; all coloring matter; and, lastly, all pabulum, including the fluid part of blood, lymph, and chyle, and corresponding matters in plants. In short, the name of bioplasm, given by Beale, or protoplasm (in a restricted sense as it will probably be ultimately accepted by biologists), as indicating the ideal living matter, cannot be given to any substance displaying rigidity in any degree, from the softest gelatinous membrane up to the hardest teeth-enamel; nor to any thing exhibiting a trace of structure to the finest microscope; nor to any liquid; nor to any substance capable of true solution. Thus, 'nothing that lives is alive in every part,' but as long as any individual part or tissue is properly called living it is only so in virtue of particles of the above-described protoplasm freely distributed among, or interwoven with the textures so closely that there is scarcely any part $\frac{1}{500}$ of an inch in size but contains its portion of protoplasm. Thus we see realized the hypothesis of Fletcher, that all living action is performed solely by virtue of portions of irritable or living matter interwoven with the otherwise dead textures. According to Beale, 'of the matter which constitutes the bodies of man and animals in the fully-formed condition, probably more than four-fifths are in the formed and non-living state. All this was, however, living at an earlier period of existence.' This is on an average, for some tissues contain much less living matter; the bones, for example, only $\frac{1}{20}$th, and some textures, when old, not more than $\frac{1}{100}$th."

I have made this long quotation from Drysdale's book, because I am anxious to do full justice to Beale, and I could not find a statement of his views so succinct for quotation in his own writing. The objection, however, urged by Bastian to Beale is so very pertinent, that it must also find a place here, but I shall not dwell upon other points on

which Beale differs from the bioplasson doctrine; such as, that living matter exhibits the same characters at every period of its existence, and, that it is always perfectly structureless. "It has always appeared to me," says Bastian,[1] "to be a very fundamental objection to his theory, that so many of the most characteristically vital phenomena of the higher animals should take place through the agency of tissues—muscle and nerve, for instance—by far the greater part of the bulk of which would, in accordance with Dr. Beale's view, have to be considered as *dead* and inert."

In 1873 the morphological knowledge of living matter became exact. In that year Heitzmann discovered the manner in which bioplasson is arranged throughout the body, and announced the fact that what had until then been regarded as separate form-elements in a tissue are really interconnected portions of living matter; that not only are there contained no isolated unit-masses in any one tissue, but no tissue in the whole body is isolated from the other tissues; and that the only unconnected particles of living matter are the corpuscular elements of liquids, such as blood, sperm, saliva, pus, etc., and so-called wandering corpuscles; so that, to use his own words: "The animal body as a whole is a connected mass of protoplasma in which, in some part, are imbedded isolated protoplasma-corpuscles (wandering corpuscles, colorless and red blood-corpuscles) and various not-living substances (glue-giving and mucin-containing substances in the widest sense, also fat, pigment-granules, etc.)." This announcement marked the commencement of a new era in biology.

Heitzmann had "investigated the condition of living matter in so-called infusions." There had at first appeared "a number of very minute granules, just perceptible to the highest powers of the microscope," granules that were homogeneous, yellowish, shining, and motionless. Such a granule represents the juvenile phase of living matter; growing larger in size it becomes vacuolized, *i. e.*, shows "a central hole, enclosed on all sides by a yellowish shining

[1] The Beginnings of Life: being some account of the nature, modes of origin, and transformations of lower organisms. London, 1872, vol. i., p. 155.

substance." "The cavities in the interior of the shining lumps, apparently filled with some fluid, differ in their refracting power from the surrounding mass; they show a slight rosy color." Still later, "some granules look as if perforated by vacuoles, like a sieve; the differentiation between the two substances within the lump—the yellowish shining and the colorless rosy-refracting—has apparently advanced." Vacuolation produces the appearance at first of a trabecular framework, and then of a filamentous network in the interior of the lump. "Such a minute transparent corpuscle, floating in the water of the infusion, constantly changes its outlines by throwing out offshoots or processes, mostly in the form of hyaline flaps; and we are sure we have an amœba before us." Heitzmann discovered that the living matter as seen in an amœba is not without structure, as had, before his accurate investigations, been supposed; and that its structure, in all cases when developed, is that of a network, in the meshes of which the bioplasson fluid, or the not-contractile, not-living portion of the organism, exists. When there is a nucleus, which may be either homogeneous (*i. e.*, compact) or vacuolized or reticulated, it is connected by delicate threads with the extranuclear network; nucleoli and nucleolini inside of the nucleus, as well as granules outside, are portions of living matter: sometimes in lump, sometimes mere points of intersection of the threads constituting the intranuclear and extranuclear living networks, sometimes terminals of section of such threads, as first explained by Eimer,[1] and after him by Klein.[2]

Heitzmann discovered that what is true of the structure of bioplasson in the amœba, where a single small unit-mass of living matter constitutes the entire individual, is true also

[1] "Weitere Nachrichten über den Bau des Zellkerns." *Archiv f. mikrosk. Anatomie*, xiv, 1877, p. 103.

[2] "Observations on the Structure of Cells and Nuclei," *Quarterly Journal of Microscopical Science*, Jan., 1879, p. 128. "The intranuclear as well as the intracellular network having, of course, three dimensions, includes fibrils that lie in the two dimensions of the plane of the field of the microscope, as well as fibrils placed vertically to it. The former appear, of course, as fibrils; but, I should like to ask, as what do the latter appear, *i. e.*, those situated vertically. Clearly as dots, because they are seen endwise; and for obvious reasons most of them lie in the nodes of the network."

of the structure of bioplasson of all, even the highest, living organisms.

It was known that the ideas originally connected with the term "cell" were erroneous, and that the essential constituent of "cells" was living matter individualized into small distinct masses; the existence in such form-elements of granules, aside from membrane, nucleus, nucleolus, and nucleolinus, was known; "thorns" and offshoots, processes and prolongations from them had even been occasionally observed; and Frommann[1] is even said[2] to have observed "clear shining fibrils proceeding from the nucleolus joining themselves to others proceeding from the nucleus and protoplasm," and to have believed "that the granules of the nucleus and protoplasm are the nodal points of a very fine fibrous network, from which fibrils go off and leave the cell." But all this knowledge was fragmentary until Heitzmann demonstrated not only that membrane, nucleus, nucleolus, granules, and threads are really the living contractile matter, but also 1) that this matter is arranged in a net work, containing in its meshes the non-contractile matter, which is transformed into the various kinds of basis-substance, characterizing different tissues; and 2) that the tissue-masses of bioplasson throughout the whole body are interconnected by means of fine threads of the same living matter.

Unless these facts of Heitzmann's discovery are accepted, there cannot be urged much against the continued use of the word "cell," misnomer though it be. Ranke,[3] after speaking of the "cell-wall," "cell-nucleus," etc., says: "Of these component parts of the cell, one or other may be wanting without the totality ceasing to be a cell. The nucleoli, the cell-wall, or the nucleus may be wanting, and yet we must designate the microscopic form a cell, or elementary organism." Now, although Drysdale thus comments upon this quotation, viz.: "If any one choose to describe a gun-barrel as a stockless gun without a lock, he is free to do so; but what

[1] "Untersuchungen über die normale und pathologische Anatomie des Rückenmarks," 2 Theil, Jena, 1867.

[2] As I have at present no access to Frommann's pamphlet, I must content myself with this expression and make the following citations from Tyson, The Cell-Doctrine: its history and present state. Philadelphia, 1878, p. 117.

[3] "Physiologie, 1872," quoted by Drysdale, *loc. cit.*, p. 104.

good purpose can it serve? Or is there even any fun in it? The truth is, this clinging to the mere name of the cell-theory by the Germans seems to arise from a kind of perverted idea of patriotism and of *pietas* toward Schwann and Schleiden." Nevertheless, I think Tyson[1] has the better of the argument, in saying: "The word has, however, become so intimately associated with histology, that it is doubtful whether it will ever fall into disuse, nor does it much matter, so long as correct notions of the elementary part are obtained." If there were any separate and distinct "elementary part," it certainly would matter little or nothing whether it were called "cell" or by any other name, provided the name be properly defined and agreed upon. It is not against the name but against the idea of any isolated individualized form-element that the objection lies. Virchow maintains[2] "that the cell is really the ultimate morphological unit in which there is any manifestation of life, and that we must not transfer the seat of real action to any point beyond the cell." Against this statement nearly every author nowadays protests, and insists that vital power must be transferred from the "cell" to "living matter"; yet, after all, the disagreement, though ever so strenuously declared, is a mere verbal one: so long as both parties hold that "every higher animal presents itself as a sum of vital unities" — no matter what these unities are called or how defined. Hæckel, one of the most avowed advocates of "the protoplasm or sarcode theory," clings to Virchow's politico-physiological comparison, that every higher organism is like an organized social community or state, in which the individual citizens are represented by the "cells" [no matter how he may define these], each having a certain morphological and physiological autonomy, although on the other hand interdependent and subject to the laws of the whole. Heitzmann's views necessitate the comparison of the body to a machine, such as a watch or a steam-engine, in which, though there are single parts, no

[1] *Loc. cit.* (see footnote 2, on p. 31), p. 128.

[2] Die Cellularpathologie in ihrer Begründung auf physiologische und pathologische Gewebelehre, Berlin, 1858, p. 3. (Translation by Chance, London, 1859, p. 3.)

part is at all autonomous, but all combine to make up one individual. According to Hæckel the body is composed of colonies of amœbæ; according to Heitzmann the body is one complex amœba.[1]

There is no better test of the truth of the bioplasson doctrine than the structure of hyaline cartilage. If hyaline cartilage consists, as "is generally believed," of "a homogeneous ground-substance in which are closed cavities harboring nucleated cells,"[2] the bioplasson doctrine is erroneous. If it merely contains lymph- or juice-channels, no matter what their character, whether open or closed, whether lined or unlined, whether in "homogeneous basis-substance," or "between layers of cells," or "in cement-substance," the bioplasson doctrine is erroneous. On the other hand, the more or less convincing observations by Frommann, Heitzmann, Hertwig, Thin, Prudden, Spina, and Flesch, that cartilage-corpuscles have offshoots, or prolongations, extending more or less far into the basis-substance, even that these prolongations anastomose with each other and connect neighboring corpuscles, are by no means sufficient to establish the doctrine. Of the three authors whose accounts are most satisfactory, Heitzmann himself, though influenced by these observations, did not depend upon them, but upon confirmatory investigations of other tissues; Spina—though he might logically have followed the consequences of his observation and reasoning—is entirely silent on the subject; and Flesch distinctly repudiates the doctrine thus: "The views here presented agree in many respects with those of Heitzmann. It shall be reserved for an intended speedy continuation of these

[1] Since this was written, even Huxley, the popular champion of protoplasm as the physical basis of life, who, as Bastian (*loc. cit.*, p. 58) says, so far back as in 1853, had put forth a powerful remonstrance against the then all-prevalent "cellular theory" of organization, has delivered an address before the International Medical Congress in London, August 9, 1881, in which he used the following language: "In fact, the body is a machine of the nature of an army, not of that of a watch, or of a hydraulic apparatus. Of this army, each cell is a soldier, etc., etc., etc.

[2] This statement of the general belief is quoted from the introductory paragraph of Thin's memoir "On the Structure of Hyaline Cartilage" (*loc. cit.*), in which Thin's own views are laid down to the effect "that layers of cells epithelial in arrangement exist in the substance of cartilage," "that both the stellate and the parallel systems of lymph-channels exist," etc.

investigations to enter into a discussion of questions concerning the general cell-doctrine. Only this I must emphasize here in opposition to Heitzmann, and in accord with Max Schultze, that the independence (selbstständigkeit) of the cell in the finished tissues does not suffer by the portrayed arrangement, although its connection, both with the surrounding basis-substance and, through the latter, with neighboring cells, is more intimate than, perhaps, appears from customary descriptions." [1]

The observations I have recorded in the second section, and especially those illustrated in figs. 4, 5, and 6, admit of but one interpretation, and that an interpretation favorable to the bioplasson doctrine. It is unnecessary to more than mention that although I have placed on record so few, I have made many different examinations, under many different circumstances, and with varying powers of amplification. I need occupy myself here with only the two fields drawn in figs. 5 and 6, with an amplification of 600 and 1200 respectively. The remarkable specimens from which they are taken show more conclusively than it was ever before shown what the structure or constitution of hyaline cartilage really is. I have explained this sufficiently under the proper heading. Its full significance now appears in its corroboration of the bioplasson doctrine. To be able to uphold the cell-doctrine, cartilage would have to be, using a homely comparison, like a cake composed of hard dough with raisins. No matter how widely we may extend the definition, to remain within the boundary of that doctrine this metaphor must be applicable. Innumerable painstaking researches have led to various modifications of notions entertained regarding the structure of these two constituents and their relation to each other. As we have seen, especially by the most recent publication on the subject, viz., that of Flesch, the acceptation of the existence in the dough of cleavage in certain directions, of interlaminary and interfibrillar spaces, and of offshoots, even ramifying prolongations of the raisin-substance, or, at all events, of an ingredient of the raisins, is held to be not

[1] *Loc. cit.*, p. 86.

incompatible with that doctrine. If, however, we can represent cartilage as a filigree or framework of raisin-substance, with here and there larger and smaller accumulations of this substance, in the meshes or interspaces of which framework blocks of dough are imbedded, certainly the fundamental view of the ultimate construction of the tissue is changed, and we are no longer in accord with the cell-doctrine, even though we be inclined to use that term in the widest possible sense.

In regard to a name as a substitute for the term "cell," I would say that all corpuscular masses may be called, simply, corpuscles. For all the accumulations of living matter within the ordinary fields of basis-substance, but more especially for those smaller masses which, having as yet developed neither a network structure nor much vacuolation, are still homogeneous, or nearly so,—I am quite willing to adopt either the designation of "plastids," proposed by Hæckel, or that of "bioplasts," proposed by Beale. Perhaps it would be best to restrict the word "bioplast" to a small mass of living matter exhibiting no differentiation, and to distinguish from it as "plastid" the larger mass showing an interior structure more or less like the fully developed corpuscle. Thus, I would always use the term "plastid" in the place of "cell."

The result, then, of my investigations as to the structure of cartilage is that in this tissue, beyond the possibility of a doubt, the living matter is arranged in the form of a network containing in its meshes the non-contractile matter. How is it with regard to the other proposition of the bioplasson doctrine, viz., that the living matter of the different tissues is interconnected? Examinations with high powers of such a specimen as that represented in fig. 1, showing the perichondrium, of horizontal sections through the larynx, or the neck, with skin and more or less of other tissues included,—and here I desire to say a word in appreciation of Dr. Carl Seiler's section-cutter, and of this gentleman's kindness in preparing some very fine sections for me,—

enable me to answer this question to the effect that fine filaments of living matter pass from one tissue to another in connection with the network of living matter in each. The details of such examinations are reserved for another publication.

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